REMARKS

Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance, which is respectfully requested.

Status of the claims

Claims 23-49 are pending in the present application. Claims 27, 29-31, 33, and 37 were previously withdrawn as drawn to a non-elected species. Applicants acknowledge with appreciation the rejoinder of claims 27, 33, and 37. Claims 23-28 and 32 -49 are presently under consideration.

By virtue of this response, claim 23 has been amended. The amendments to claim 23 are supported by the specification, in general throughout Example VI, for example, on page 57, line 27, and in Figures 29, 31, and 32, and on page 50, lines 6-8. No new matter has been added by the foregoing amendments.

Applicants reiterate their request for inclusion of withdrawn species upon allowance of a generic claim, as permitted by 37 C.F.R. §1.141(a).

Applicants have not dedicated to the public or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Rejections under 35 U.S.C. §112, second paragraph

Claims 23-28 and 32-49 are rejected under 35 U.S.C. §112, second paragraph, as allegedly incomplete for omitting essential steps, such omission amounting to a gap between the steps. Applicants respectfully traverse the rejection.

The Examiner states that the claimed method is indefinite because it is not apparent that there is a correlation between the "catalytic action upon the substrate" recited in step (a) and the "detection of the presence of the target molecule" as recited in step (b). Applicants respectfully submit that the claim is clear as written. However, to expedite prosecution, claim 23 has been

amended to recite "detecting said catalytic action" in step (b), thus providing a correlation between the steps of the method.

The Examiner also states that the phrase "if any" questions the presence and/or absence of the target molecule in the composition, whereas the method is directed to a method for detecting the presence of a target molecule, and is not drawn to a method for detecting the presence and/or absence of a target molecule in a composition. Applicants respectfully disagree with this statement. Inherently, a method that detects the presence of a target molecule would also detect the absence of the target, if no catalytic action is observed. However, claim 23 as amended no longer recites this phrase, rendering the rejection moot.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

Rejection under 35 U.S.C. §102(e)

Claims 23-26, 27-28, 33, and 37 are rejected under 35 U.S.C. §102(e) as allegedly anticipated by Bekkaoui et al. (U.S. Patent No. 6,136,533) for reasons of record and those set forth in the present Office Action. Applicants respectfully traverse this rejection.

The Examiner states that the features upon which Applicants rely, specifically with regard to allosteric regulation of the claimed RNA molecule, are not recited in the rejected claims. Applicants respectfully disagree with this statement. The claims recite that binding of a catalytically inactive RNA molecule to a target allows catalytic action upon a substrate other than the target. This recited change in the claimed RNA upon binding to a target, from a catalytically inactive state to having the ability to perform catalysis, is allosteric regulation. Thus, although the words "allosteric regulation" are not specifically used, allosteric regulation is nonetheless recited in the claims. However, solely to further clarify the claims and highlight the allosteric nature of the claimed catalytic process, claim 23 has been amended to recite that the catalytic action upon the substrate is *dependent* upon binding of the catalytically inactive RNA molecule to the target.

The Examiner discusses the disclosure at column 13, line 46 - column 14, line 3 of Bekkaoui et al. as teaching use of a ribozyme for detection of a target nucleic acid molecule in the presence of a labelled heterologous nucleic acid molecule (termed "co-target") in solution. Applicants respectfully note that this passage of Bakkoui et al. discloses "a ribozyme molecule" generally but does not teach a *catalytically inactive RNA molecule* as claimed. There is also no teaching of catalytic action of an RNA molecule upon a substrate which is *dependent on target binding* as claimed. Since the cited reference does not teach these two claim elements, it does not anticipate the pending claims.

Bekkaoui et al. is not enabling for target-dependent catalysis as claimed. There is no disclosure of nucleic acid sequences or reaction conditions which would enable one of skill in the art to make and use an RNA construct for target-dependent catalysis towards a substrate in a method for detection of a target molecule as claimed. No experimental data or figures are provided to teach one of skill in the art how to make and use such a construct or perform such a method. All of the working examples involve RNase H, a non-allosterically regulated protein enzyme. Bekkaoui et al. do not exemplify an allosterically regulated ribozyme in their working examples and do not provide sufficient information in their detailed description to enable one of skill in the art to practice the presently claimed invention. Thus, Applicants respectfully maintain that the disclosure at column 13, line 46 - column 14, line 3 is not an enabling disclosure with regard to the target detection methods as presently claimed.

Further, Bekkaoui et al. teach a target detection method comprising providing ribosomal protein, and/or spermine, and/or a chelator and a detergent in the reaction mixture (column 13, lines 48-50). These components are neither required nor claimed in the present invention. Bekkaoui et al. do not teach a detection method that does not require ribosomal protein, spermine, or a chelator and detergent as components of the detection system, in contrast to the presently claimed invention.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(e).

Rejection under 35 U.S.C. §102(b)

Claims 23-26, 27, 32, 33, and 37-40 are rejected under 35 U.S.C. §102(b) as allegedly anticipated by Stefano (U.S. Patent No. 5,472,840) for reasons of record and those set forth in the present Office Action. Applicants respectfully traverse this rejection.

The Examiner states that "the RNA target molecule 11 of Figure 1A of Stefano comprises a region 29 that forms the catalytic region of a ribozyme, *once bound to the first nucleic acid 31*." Office Action, page 5, emphasis added. Thus, target nucleic acid sequences, in particular the sequence GAAA, form part of the catalytic domain in the construct of Stefano (see Figure 1A, region of target nucleic acid between numerals 27 and 29). In the construct described in Figure 1A, a nucleic acid that includes only a portion of a ribozyme catalytic domain requires binding to a target nucleic acid which provides the remainder of the sequences of a complete catalytic domain, as the Examiner herself has stated in the Office Action. In contrast, the presently claimed invention provides a catalytically inactive RNA that includes all nucleotide sequences of a complete catalytic domain *in the absence of target sequences*. No binding to target sequences is necessary to form the complete catalytic domain of the ribozyme, in contrast to the construct described in Figure 1A of Stefano. In the presently claimed invention, the claimed catalytically inactive RNA molecule that binds to a target comprises all of the nucleotide sequences of a complete catalytic domain *before* binding to the target. In the claimed invention, the target sequences stabilize the active conformation of the ribozyme, but do not participate in formation of the catalytic domain itself.

Applicants distinguished their invention over Stefano at page 61, lines 13-25 of the specification. Applicants described the European counterpart to Stefano, EP 0 707 076, as disclosing a ternary hybrid formed between a latent MDV-1 RNA substrate, a second RNA probe, and a target RNA to produce an autocatalytic hammerhead ribozyme. Among the disadvantages of this system as described by Applicants is that this method "is limited to *target sequences that contain the element GAAA* (required to generate an active hammerhead ribozyme)." Page 61, lines 22-24, emphasis added. In contrast, as discussed above, the claimed invention includes the nucleotide sequences of a complete catalytic domain that is separate from and independent of target sequences. Figures 31 and 32 of the instant application show RNA constructs according to the

present invention that include a complete catalytic domain, identical in sequence to the catalytic domain shown in Figure 1A of Stefano, but wherein target sequences are separate from and do not form part of the catalytic domain. In Figures 31 and 32, the GAAA sequence is part of the catalytic domain of the ribozyme construct, but is not part of the target sequence, in contrast to Stefano.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b).

Withdrawn rejections

Applicants acknowledge with appreciation the withdrawal of the previous rejection under 35 U.S.C. §112, first paragraph.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 367592000100. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: May 3, 2004

Respectfully submitted,

By Jill A. Jacobson

Jill A. Jacobson
Registration No.: 40,030
MORRISON & FOERSTER LLP
755 Page Mill Road
Palo Alto, California 94304
(650) 813-5876